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CLINICAL REVIEW

Short sleep duration predicts risk of metabolic syndrome: A systematic review and meta-analysis

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SUMMARY

Sleep duration has been suggested to play a key role in the development of metabolic syndrome (MS). However, the results have been inconsistent. The objective of this study was to clarify the association between sleep duration and MS risk. PubMed and Embase databases were searched for eligible publications. Pooled odds ratio (OR) with 95% confidence interval (CI) was calculated using random- or fixed-model. A total of 12 studies (18,720 MS cases and 70,833 controls) were included in the meta-analysis. Short sleep duration was significantly associated with increased risk of MS (OR = 1.27, 95%CI = 1.09–1.47, $p = 0.002$). Long sleep duration was not associated with increased risk of MS (OR = 1.07, 95%CI = 0.87–1.32, $p = 0.535$). Similar results were found in both men and women. The sensitivity analysis confirmed the stability of the results and no publication bias was detected. The present meta-analysis suggests that short rather than long sleep duration is significantly associated with risk of MS. Large-scale well-design prospective studies are required to further investigate the association between sleep duration and MS risk.

Introduction

Chronic sleep deprivation is becoming epidemic worldwide. Recent meta-analyses have indicated that there is a U-shaped relationship between sleep duration and obesity,[1] hypertension,[2] type 2 diabetes,[3] cardiovascular outcomes (including coronary heart disease, stroke and total cardiovascular disease (CVD))[4] and all-cause mortality.[5] These data suggest that sleep duration might be associated with increased risk of metabolic syndrome (MS).

MS is a constellation of metabolic abnormalities including obesity, hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol and hyperglycemia. Based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII) criteria, three of these components characterize MS. Since MS increases the risk of type 2 diabetes, CVD and all-cause mortality,[6] it is important to identify the risk factors of MS and to early prevent and control MS. The traditional lifestyle factors such as diet and physical activity may not fully account for the development of MS. To date, about 10 papers have been published to investigate the association between sleep duration and MS risk.[7–16] However, the results have been inconsistent. Taking short sleep duration for example, five papers suggested it was positively associated with MS,[7,9–11,14] while other papers indicated non-significant association.[10,12–16] The discrepancy might be due to the insufficient statistical power of individual studies.

Therefore, in this study, we performed a meta-analysis to clarify the association between sleep duration and MS risk.

Materials and methods

Literature and search strategy

Literature databases were searched including PubMed and Embase. The search strategy to identify all possible studies involved the use of the following key words: "sleep" and ("metabolic syndrome" or "MetS" or "MS" or "metabolic syndrome X" or "syndrome X" or "cardiometabolic risk factor" or "insulin resistance syndrome"). The reference lists of retrieved articles were hand-searched. The literature search was limited to English language. If more than one article were published using the same data, only the study with largest sample size was included. The literature search was updated on December 15, 2012.

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; HDL, high density lipoprotein; MS, metabolic syndrome; NCEP ATPIII, National Cholesterol Education Program Adult Treatment Panel III; OR, odds ratio; RR, relative risk.

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Inclusion criteria and data extraction

The studies included in the meta-analysis must have met all the inclusion criteria: 1) evaluated the association between sleep duration and MS; 2) used case-control or cohort design; 3) provided sufficient data for calculation of odds ratio (OR) or relative risk (RR) with 95% confidence interval (CI). The following information was extracted from each study: 1) name of the first author; 2) year of publication; 3) country of origin; 4) number of subjects in MS cases and controls; 5) sex ratio and mean age of the study population; 6) study design; 7) sleep duration category; 8) MS criteria; 9) covariates used in adjustment. Two authors independently assessed the articles for compliance with the inclusion/exclusion criteria and resolved disagreements through discussion.

Statistical analysis

The association of short or long sleep duration with MS was estimated by calculating pooled OR and 95%CI. The significance of pooled OR was determined by Z test ($p < 0.05$ was considered statistically significant). A Q test was performed to examine the between-study heterogeneity. A random- (DerSimonian–Laird method[17]) or fixed- (Mantel–Haenszel method[18]) effects model was used to calculate pooled OR in the presence ($p \leq 0.10$) or absence ($p > 0.10$) of heterogeneity, respectively. Subgroup analysis based on sex was conducted. Sensitivity analysis after excluding one study at a time was performed to assess the stability of the results. Publication bias was assessed by Begg's test[19] and Egger's test[20] ($p < 0.05$ was considered statistically significant). Statistical analysis was conducted using STATA version 11 (StataCorp LP, College Station, Texas, USA).

Results

Characteristics of the studies

A flow chart of meta-analysis for exclusion/inclusion of individual articles (or studies) is presented as Fig. 1. The literature search identified a total of 297 potentially relevant papers. 276 papers were excluded after reading the title and abstract because of obvious irrelevance. Four reviews and two papers published in Japanese or Chinese were also excluded. Two papers were excluded since they examined the association between sleep duration and components of MS. In addition, three papers[21–23] were excluded because they did not provide OR (or RR) with 95%CI or sufficient data for calculation of it. Thus, 10 papers met the inclusion criteria.[7–16] Since the data were provided by sex in two papers, they were considered as separate studies in the subsequent data analysis. Therefore, 12 studies (18720 MS cases and 70833 controls)[7–16] were included in the final meta-analysis. Of them, 10 studies were cross-sectional based and two were cohort based; 10 studies used NCEP ATPIII criteria to define MS, one used the Japanese Guidelines and the rest one used the Consensus Statement Guidelines. Sleep duration category (h) and other characteristics of the included studies are presented in Table 1.

Meta-analysis results

Short sleep duration was significantly associated with increased risk of MS (OR = 1.27, 95%CI = 1.09–1.47, $p = 0.002$; Fig. 2 and Table 2) with evidence of between-study heterogeneity ($I^2 = 76.4\%$, p for heterogeneity <0.001). The effect in men (OR = 1.24, 95% CI = 1.04–1.46, $p = 0.013$) and women (OR = 1.35, 95%CI = 1.00–1.81, $p = 0.048$) was similar (Table 2).

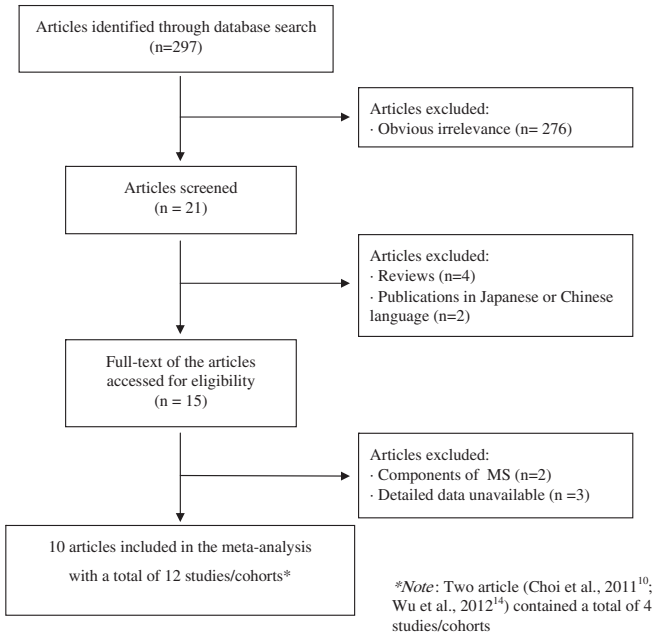

Fig. 1. Flow chart of meta-analysis for exclusion/inclusion of individual articles (or studies).

Long sleep duration was not associated with increased risk of MS (OR = 1.07, 95%CI = 0.87–1.32, $p = 0.535$; Fig. 3 and Table 2) with evidence of between-study heterogeneity ($I^2 = 80.9\%$, p for heterogeneity <0.001). A similar non-significant association was found in men (OR = 1.09, 95%CI = 0.66–1.79, $p = 0.732$) and women (OR = 0.87, 95%CI = 0.75–1.01, $p = 0.066$) (Table 2).

Sensitivity analysis and publication bias

After excluding one study at a time, the sensitivity analysis confirmed the significant association between short sleep duration and risk of MS (OR with 95%CI ranging from 1.23 (1.06–1.43) to 1.33 (1.19–1.48)). No publication bias was detected for short sleep duration (Begg's test: $p = 0.631$ and Egger's test: $p = 0.297$) and long sleep duration (Begg's test: $p = 0.945$ and Egger's test: $p = 0.840$).

Discussion

To our knowledge, the present study represents the first meta-analysis quantitatively investigating the association between sleep duration and risk of MS. We found that short sleep duration was significantly associated with risk of MS; long sleep duration might not be associated with MS. Further stratification for sex demonstrated similar trends. Our study recruited a total of 18,720 MS cases and 70,833 controls, which greatly improved the statistical power and the conclusions were more credible than those of individual studies. The sensitivity analysis further confirmed the stability of the conclusions. In addition, we extracted the covariates' adjusted OR (or RR) with 95%CI from each study and pooled them with meta-analysis. Thus, the potential confounders including age, sex and body mass index etc. were controlled for.

Several meta-analyses supported the association between sleep duration and obesity,[1,24] hypertension[2] and type 2 diabetes.[3] Since obesity, hypertension and impaired fasting glucose are components of MS, it is not surprising that short sleep duration was positively associated with MS. For the association between sleep duration and

Table 1
Characteristics of the studies included in the meta-analysis.

Study	Country	No. of cases	No. of controls	Sex (male, %)	Age (mean ± SD, y)	Study design	Sleep duration category (h)	Metabolic syndrome criteria	Adjustment[a]
Hall et al., 2008[7]	US	272	942	46.6	44.4 ± 6.8	Cross-sectional	Referent = 7–8 Short = <6 Long = >8	NCEP ATPIII	1, 2, 3, 4, 5, 6, 7, 8
Choi et al., 2008[8]	Korea	1100	2905	43.1	44.1 ± 4	Cross-sectional	Referent = 7 Short = ≤5 Long = ≥9	NCEP ATPIII	1, 2, 4, 5, 6, 9, 10, 11, 12
Najafian et al., 2011[9]	Iran	2936	9556	48.9	38.9 ± 14.9	Cross-sectional	Referent = 7–8 Short = ≤5 Long = >8	NCEP ATPIII	1, 2
Choi et al., 2011 (male)[10]	Korea	82	304	All were male	49 ± 4	Cohort	Referent = 6–8 Short = <6 Long = ≥10	NCEP ATPIII	1, 5, 6,12,13, 14
Choi et al., 2011 (female)[10]	Korea	122	599	All were female	48 ± 4	Cohort	Referent = 6–8 Short = <6 Long = ≥10	NCEP ATPIII	1, 5, 6,12,13, 14
Kobayashi et al., 2011[11]	Japan	2418	25,374	49.5	48.8 ± 12.8	Cross-sectional	Short = <6 Long = ≥8	The Japanese Guidelines	1, 2, 5, 6, 12, 15, 16
Arora et al., 2011[12]	China	8222	21,111	72.4	50–96 (age range)	Cross-sectional	Referent = 7–8 Short = <6 Long = ≥9	The Consensus Statement Guidelines	1,2,4, 5, 6, 9, 17, 18, 19, 12, 20, 21,22,23, 24
Sabanayagam et al., 2012[13]	US	2284	3838	49.9	44.6 ± 6	Cross-sectional	Referent = 7 Short = ≤5 Long = ≥9	NCEP ATPIII	1,2,3, 4, 5, 6, 8, 12
Wu et al., 2012 (male)[14]	China	760	3538	All were male	45 ± 11	Cross-sectional	Referent = 6–8 Short = <6 Long = >8	NCEP ATPIII	1, 4, 5, 6, 12, 13
Wu et al., 2012 (female)[14]	China	275	2527	All were female	45 ± 11	Cross-sectional	Referent = 6–8 Short = <6 Long = >8	NCEP ATPIII	1, 4, 5, 6, 12, 13
McCanlies et al., 2012[15]	US	14	84	60.2	39.6 ± 7	Cross-sectional	Short = <6 Long = >6	NCEP ATPIII	1, 2, 4, 5
Hall et al., 2012[16]	US	235	105	All were female	46–57 (age range)	Cross-sectional	As continuous variable	NCEP ATPIII	3, 4, 5, 6, 9,12, 13, 14, 25, 26

NCEP ATPIII, National Cholesterol Education Program Adult Treatment Panel III criteria.
[a] 1, age; 2, sex; 3, race; 4, education; 5, smoking; 6, physical activity; 7, LDL-cholesterol; 8, depression; 9, family history of hypertension or diabetes; 10, residential area; 11, monthly income; 12, alcohol intake; 13, body mass index; 14, menopause (female); 15, myocardial infarction; 16, cerebral infarction; 17, insomnia; 18, use of hypnotics; 19, daytime sleepiness; 20, snoring; 21, systolic blood pressure; 22, glucose; 23, total cholesterol; 24, triglycerides; 25, marital status; 26, use of medications that affect sleep.

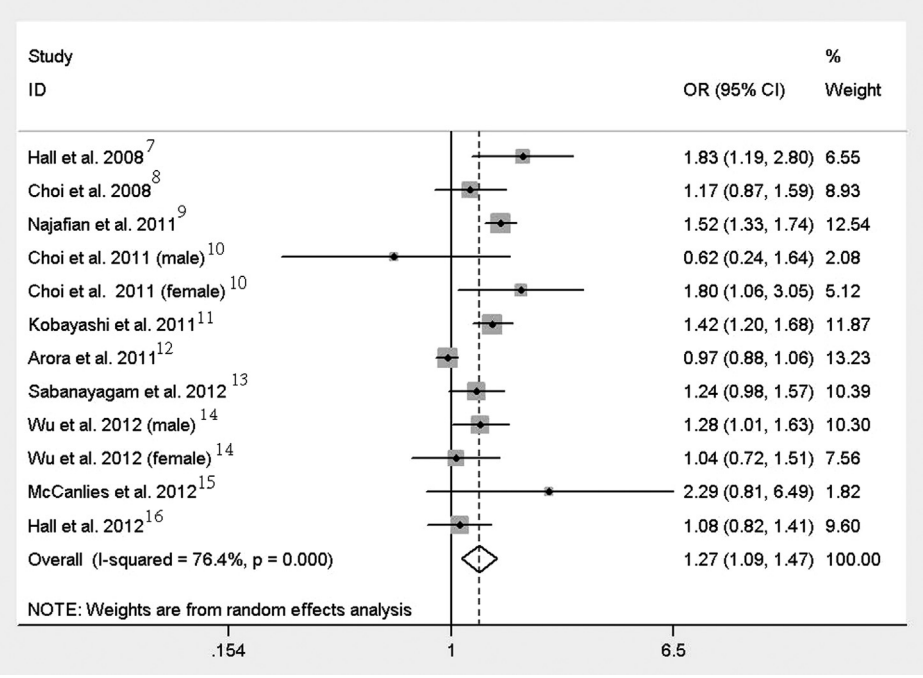

Fig. 2. Meta-analysis of the association between short sleep and risk of metabolic syndrome.

Table 2
Meta-analysis of the association between sleep duration and metabolic syndrome.

	No. of studies	OR	95%CI	P_Z	Statistical model	I^2 (%)	P_H
Short sleep							
All	12	1.27	1.09–1.47	0.002	Random	76.4	<0.001
Sex							
Male	3	1.24	1.04–1.46	0.013	Fixed	3.4	0.355
Female	4	1.35	1.00–1.81	0.048	Random	73.9	0.009
Long sleep							
All	12	1.07	0.87–1.32	0.535	Random	80.9	<0.001
Sex							
Male	3	1.09	0.66–1.79	0.732	Random	56.9	0.098
Female	4	0.87	0.75–1.01	0.066	Fixed	0.1	0.391

Abbreviations: OR, odds ratio; CI, confidence interval.
P_Z, *P* value for *Z* test.
P_H, *P* value based on *Q* test for between-study heterogeneity.

obesity, two meta-analyses[1,24] and two systematic reviews[25,26] have been published. Although the above four articles included somewhat different studies, they all indicated a positive association of short sleep duration with obesity risk.[1,24–26]

The biological mechanism underlying the association between short sleep duration and MS risk is still unclear. It is suggested that short sleep duration increases body weight and changes glucose metabolism.[7] In experimental studies, inadequate sleep significantly changes the main components of energy homeostasis, including glucose tolerance, food craving, and hormones critical to appetite regulation.[27] For instance, sleep restriction could reduce leptin and elevate ghrelin, which regulate satiety and hunger, respectively,[28] thereby increasing the cravings for calorie-dense and carbohydrate-rich food.[29]

Our study is subject to several limitations. First, all included studies measured sleep duration using subjective questionnaires rather than objective actigraphy. However, self-reported sleep duration assessment is well correlated with values obtained by actigraphic monitoring.[30] Second, there was evidence of between-study heterogeneity for the association between short or long sleep duration and MS risk. Thus, we used meta-regression analysis to examine the source of heterogeneity. The following independent variables including publication year, sex ratio and mean age in cases and controls, study design, and MS criteria were introduced into the meta-regression model. However, these variables can not explain the source of heterogeneity, suggesting that other unknown confounding variables might be the source of heterogeneity. Third, the confounding variables controlled for were different between studies. Further well-designed studies with consideration of more covariates are required to examine the association between sleep duration and MS risk. Fourth, in the present meta-analysis, we did not pay attention to the association of obstructive sleep apnoea and sleep quality (e.g., difficulty in initiating sleep and in maintaining sleep), with MS risk. Further meta-analyses are required to clarify these associations. Fifth, the included studies were mostly performed in Asia and US. The findings might not be extended to populations of other ethnicity. In addition, criteria for MS were different for the included studies. However, the results did not significantly change after exclusion of two studies which did not use NCEP ATPIII criterion.[11,12] Sixth, cross-sectional study design was used for the majority of the included studies, which could not allow for causal inference. Thus, longitudinal studies are required to assess whether a cause–effect relationship may exist between short sleep duration and development of MS. In addition, further data should be obtained in young populations as the current results were mainly based on older populations with age more than 40 y old.

In summary, the present meta-analysis suggests that short rather than long sleep duration is significantly associated with risk of MS. Similar results were found in both men and women. The findings of our study have great public health significance: it will be important to recommend people sufficient sleep time to prevent and control MS, in order to ultimately reduce the risk of type 2 diabetes, CVD and all-cause mortality. However, large-scale well-designed prospective studies are necessary to be conducted to

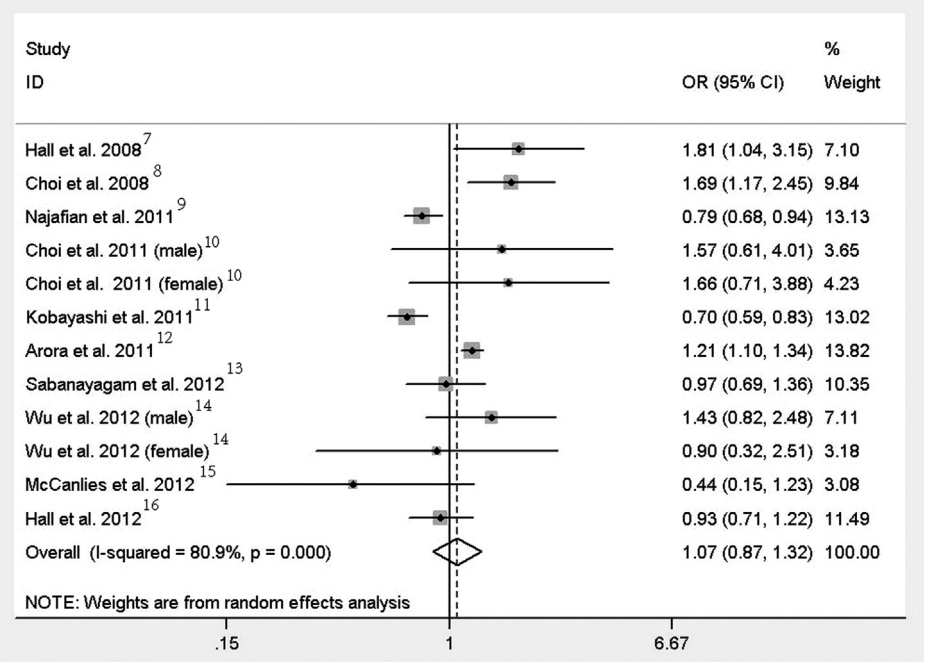

Fig. 3. Meta-analysis of the association between long sleep and risk of metabolic syndrome.

further confirm the association between sleep duration and MS risk.

Practice points

1) Sleep duration has been suggested to play a key role in the development of metabolic syndrome. However, the results have been inconsistent.
2) Short sleep duration was significantly associated with increased risk of metabolic syndrome (odds ratio = 1.27, 95% confidence interval = 1.09–1.47, $p = 0.002$).
3) Long sleep duration was not associated with increased risk of metabolic syndrome (odds ratio = 1.07, 95% confidence interval 0.87–1.32, $p = 0.535$).

Research agenda

1) Habitual sleep duration should be measured using objective actigraphy rather than subjective questionnaire.
2) Large-scale well-designed prospective studies with consideration of more confounding factors are necessary to further confirm the association between sleep duration and metabolic syndrome risk.
3) The biological mechanism underlying the association between short sleep duration and metabolic syndrome risk needs to be examined.

Conflicts of interest

The authors have declared that no competing interests exist.

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